TITLE: Preparation of pyrazoles and analogs as PPAR modulators for treatment of metabolic disorders, diabetes mellitus, atherosclerosis, and cardiovascular disorders

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PATENT ASSIGNEE(S): Eli Lilly and Company, USA

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RW:	BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003296404	A1	20040810	AU 2003-296404	20031231
EP 1585733	A1	20051019	EP 2003-815195	20031231
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, BG, CZ, EE, HU, SK			
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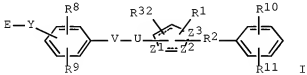
GI



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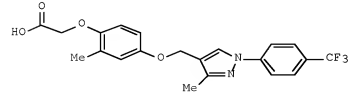


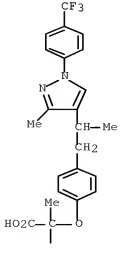
II

AB Title pyrazoles, imidazoles, and (is)oxazoles I [wherein R1 = H, (un)substituted alkyl, alkenyl, (hetero)aryl(alkyl), arylheteroalkyl, cycloalkylaryl(alkyl); R2 = absent, (hetero)alkyl; R8 = H, alkyl, alkylenyl, halo; R9 = H, (un)substituted alkyl, alkylenyl, halo, aryl(alkyl), heteroaryl, allyl, alkoxy, alkylthio, etc.; R10, R11 = independently H, OH, CN, NO2, halo, oxo, (un)substituted (halo)alkyl, alkoxy, cycloalkyl, (hetero)aryl(alkyl), cycloalkylaryl(alkyl), aryloxy, acyl, carboxy, amino, sulfamoyl, etc.; R32 = bond, H, halo, (halo)alkyl, alkyloxo; E = (un)substituted carboxy(methyl), tetrazolyl(methyl), nitriloalkyl, carboxamido(methyl), sulfonamido(methyl); U = (un)substituted aliphatic linker wherein one C of the linker is optionally replaced with O, NH, or S; X = bond, O, S, SO2, NH; Y = bond, CH2, NH; Z1, Z2 = independently N, O, C, whit the proviso that at least one of Z1 and Z2 = N; Z3 = N, O, C; or stereoisomers, pharmaceutically acceptable salts, solvates, and hydrates thereof] were prepared as peroxisome proliferator activated receptor (PPAR) modulators (no data). For example, chlorination of [3-methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]methanol with MeSO2Cl and TEA in CH2Cl2, followed by coupling with (4-hydroxy-2- methylphenoxy)acetic acid Me ester using Cs2CO3 in acetonitrile and saponification with NaOH in MeOH provided II. I and their pharmaceutical compns. are expected to be effective in treating and preventing metabolic disorders, diabetes mellitus, atherosclerosis, and cardiovascular disorders (no data).

IT 728913-16-4P, 2-Methyl-2-[4-[2-[3-methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]propyl]phenoxy]propionic acid 728914-84-9P, [4-[2-[3-Methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]ethyl]phenoxy]acetic acid 728914-85-0P, 2-Methyl-2-[4-[2-[3-methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]ethyl]phenoxy]propionic acid 728914-86-1P, [4-[2-[3-Methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]propyl]phenoxy]acetic acid
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(PPAR modulator; preparation of pyrazoles and analogs as PPAR modulators for
treatment of metabolic disorders, diabetes, atherosclerosis, and cardiovascular disorders)

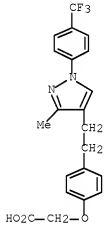
RN 728913-16-4 CAPLUS

CN Propanoic acid, 2-methyl-2-[4-[2-[3-methyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]propyl]phenoxy]- (CA INDEX NAME)



Me

RN 728914-84-9 CAPLUS
CN Acetic acid, 2-[4-[2-[3-methyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]ethyl]phenoxy]- (CA INDEX NAME)



RN 728914-85-0 CAPLUS
CN Propanoic acid, 2-methyl-2-[4-[2-[3-methyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]ethyl]phenoxy]- (CA INDEX NAME)

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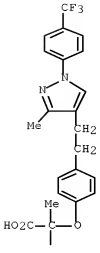

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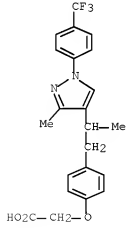
Me

RN 728914-86-1 CAPLUS
CN Acetic acid, 2-[4-[2-[3-methyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]propyl]phenoxy]- (CA INDEX NAME)



IT 728914-90-7P, [4-[2-[3-Methyl-1-(4-trifluoromethylphenyl)-1H-pyrazol-4-yl]propyl]phenoxy]acetic acid methyl ester
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; preparation of pyrazoles and analogs as PPAR modulators for treatment of metabolic disorders, diabetes, atherosclerosis, and cardiovascular disorders)

RN 728914-90-7 CAPLUS

CN Acetic acid, 2-[4-[2-[3-methyl-1-[4-(trifluoromethyl)phenyl]-1H-pyrazol-4-yl]propyl]phenoxy]-, methyl ester (CA INDEX NAME)

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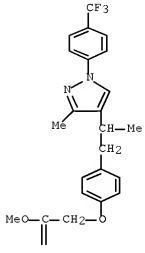

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